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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/780,905	02/18/2004	Daniel Paris	4303-040164	7571

28289 7590 12/08/2005

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EXAMINER

CORDERO GARCIA, MARCELA M

ART UNIT	PAPER NUMBER
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1654

DATE MAILED: 12/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/780,905

Applicant(s)

PARIS ET AL.

Examiner

Marcela M. Cordero Garcia

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1654

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 October 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5, 25, 20-29 and 40-41, 45-59 is/are pending in the application.
- 4a) Of the above claim(s) 4-5 and 28-29 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3, 6, 7, 15, 20-27, 30, 31, 40, 41 and 45-59 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 0405.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to the reply received on October 3, 2005.

Claims 1-5, 15-29 and 39-49 are pending in the application.

Claims 16-19, 39 and 42-44 have been cancelled.

Claims 50-59 have been added.

Any rejection from the previous office action, which is not restated here, is withdrawn.

Accordingly, claims 1-5, 15, 20-29, 40-41 and 45-49 (readable on the elected species, i.e., a method of treating a tumor using L-685,458) are presented for examination on the merits.

Claims 1-5, 15, 20-29, 40-41 and 45-49 have been examined and found free of the prior art.

A new species from amongst those encompassed by the instant claims has been elected by Examiner, namely, a method of treating a tumor using DAPT. Claims 1-3, 6-7, 15, 20-27, 30-31, 40-41, 45-59 are readable thereon.

Claims 1-3, 6-7, 15, 20-27, 30-31, 40-41, 45-59 are presented for examination on the merits as far as they read upon a method of treating a tumor using DAPT.

Specification

The disclosure stands objected to because of the following: This application contains sequence disclosures that are encompassed by the definitions for nucleotide

and/or amino acid sequences set forth in 1(a)(1) and (a)(2) (see, e.g., paragraph 52 of the instant application publication [US 2004/0229816] and/or disclosure, page 13, paragraph [49]). Therefore, this application fails to comply with the requirements of 37 CFR §§ 1.821 through 1.825. Appropriate correction is required.

Although Applicant submitted a CRF and sequence listing in response to this objection, the application is still not in compliance as indicated in a Notice to Applicant mailed out on October 12, 2005.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 6-7, 15, 20-27, 30-31, 40-41, 45-59 are rejected under 35

U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

The amended claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant has amended the claims from 'administering therapeutically effective amounts *in unit form*' to 'administering to the animal or human a therapeutically effective amount'. There is no support in the specification for the broadening of this limitation (see, e.g., paragraphs [22]-[23], [40]-[41] of the publication

of the instant application [US 2004/0229816], and/or see disclosure, e.g., page 10, paragraphs [20]-[21], [38]-[39]).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6-7 and 30-31 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter which applicant(s) regard as their invention.

Claim 6 and 30 are rendered vague and indefinite by the phrase "R refers to analogue substitutions" because the nature of R (e.g., bond, functional group, molecule, atom, electron pair) is not defined, and it is also not clear to what is the R substitution analogue to. Further, R₂ is also present and not defined. The metes and bounds of the claimed invention are not clearly delimited in order to determine a potential infringement upon the instantly claimed invention.

All other claims that depend directly or indirectly from rejected claims and are, therefore, also rejected under USC 112, second paragraph for the reasons set forth above.

Claims 1-3, 6-7, 15, 20-27, 30-31, 40-41 and 45-59 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for specific secretase inhibitors such as L-685,458, DAPT and DAPM, JLK-6, OM99-2, Z-VLL-CHO, GL189 and P10-P4'statV, does not reasonably provide enablement for any and all secretase inhibitors. The specification does not enable any person skilled in the art to

which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims, which includes any and all protease inhibitors.

With regards to protease inhibitors and their properties, the art is unpredictable. Shearman et al. (Biochem, 2000) state, "Specific and potent inhibitors of A β PP (amyloid beta-protein precursor) gamma secretase activity such as L-685,458 will enable important advances toward the identification and elucidation of the mechanism of action of this *enigmatic* protease".

Further, as Applicant readily admits in page 13 of their reply dated September 30, 2005, "the mechanism by which gamma secretase inhibitors inhibit angiogenesis may not be via inhibition of Notch signaling in endothelial cells at all, but due to some other, as yet unidentified mechanism".

Given that one could not determine a general mechanism of anti-angiogenic action for all protease inhibitors, that gamma proteases themselves are highly enigmatic, and given the breadth of the working examples provided, it flows logically that one would be unduly burdened with experimentation to determine the effect of any and all protease inhibitors (including any proteases created by substitution of groups therein) in regards to their anti-angiogenic properties and in order to use/make the instantly claimed therapeutic invention.

All other claims that depend directly or indirectly from rejected claims and are, therefore, also rejected under USC 112, second paragraph for the reasons set forth above.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-3, 6-7, 25-27, 30-31, 40-41, 59 are rejected under 35 U.S.C. 102(a) as being anticipated by Jundt et al. (Blood, November 16, 2002, Vol. 100, No. 11, PG-Abstracts No. 594, page 158a).

Jundt et al. teach a method of treating a tumor in an animal or human in need of such treatment by inhibiting angiogenesis comprising administering to the animal or human a therapeutically effective amount of a composition comprising a carrier and at least one secretase inhibitor effective to inhibit angiogenesis and to reduce tumor volume in said animal or human. (See Jundt et al: abstract, page 158a).

Therefore, the reference is deemed to anticipate the instant claims above.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

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the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, 6-7, 15, 20-27, 30-31, 40-41, 45-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jundt et al. (Blood, November 16, 2002)

Jundt et al. beneficially teach a method of treating a tumor by inhibiting angiogenesis comprising administering to the animal or human a therapeutically effective amount of a composition comprising a carrier and at least one secretase inhibitor effective to inhibit angiogenesis and to reduce tumor volume. (See entire abstract, Blood 2002, Vol. 100, No. 11, page 158a).

Jundt et al. do not expressly teach an in vivo method of treating a tumor in an animal or human in need thereof and using a carrier in addition to the secretase inhibitor. It would have been obvious to one of ordinary skill in the art at the time the invention was made to adjust particular conventional working conditions within such method of treating cancer (e.g., expressly carrying out in vivo administration of such inhibitors using various modes of administration known in the art and/or treating different types of tumor growths) based upon the overall beneficial teachings provided by Jundt et al. (see, e.g., last paragraph indicating that in vivo studies are being carried out to determine whether DAPT inhibits cell growth in vivo and that the use of such

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inhibitors might be a novel therapeutic principle to control the proliferation capacity of neoplasms (i.e., tumors in general). These types of adjustments are deemed merely a matter of judicious selection and routine optimization that is well within the purview of the skilled artisan.

Thus, the invention as a whole is prima facie obvious over the reference, especially in the absence of evidence to the contrary.

Claims 1-3, 6-7, 15, 20-27, 30-31, 40-41, 45-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weng et al. (Mol. Cell. Biol., January 2003).

Weng et al. beneficially teach a method of treating a tumor by inhibiting angiogenesis comprising administering to the animal or human a therapeutically effective amount of a secretase inhibitor effective to inhibit angiogenesis and to reduce tumor volume. (See, e.g., abstract, page 656, column 2, lines 28-38, 57-75, page 657, column 1, lines 2-6, 23-35, page 662, column 2, lines 13-16, page 663, column 1, lines 1-59, column 2, lines 1-17, Figs. 2-8).

Weng et al. do not expressly teach an in vivo method of treating a tumor in an animal or human in need thereof and using a carrier in addition to the secretase inhibitor and/or expressly selecting DAPT from amongst the secretase inhibitors listed therein.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to adjust particular conventional working conditions within such method of treating cancer (e.g., expressly selecting DAPT as the secretase inhibitor, carrying out in vivo administration of such inhibitors using various modes of

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administration known in the art and/or treating different types of tumor growths) based upon the overall beneficial teachings provided by Weng et al. since Weng teaches that DAPT and analogous secretase inhibitors specifically induce growth suppression and apoptosis of murine pre-T acute lymphoblastic leukemia cells in vitro and that this step is a potential target for chemotherapeutic intervention. (See citations above). These types of adjustments are deemed merely a matter of judicious selection and routine optimization that is well within the purview of the skilled artisan.

Thus, the invention as a whole is prima facie obvious over the reference, especially in the absence of evidence to the contrary.

Conclusion

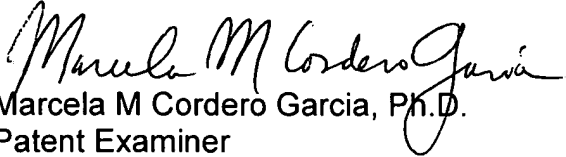
No claim is allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marcela M Cordero Garcia whose telephone number is (571) 272-2939. The examiner can normally be reached on M-Th 7:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


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MMCG 11/05


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